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DENTAL COMPOSITIONS AND METHODS OF MAKING SAME

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This application is a continuation-in-part of application Ser. No. 753,609, filed Aug. 7, 1958, now abandoned. The invention is directed primarily to pharmaceutical compositions, particularly those which are useful in the treatment of "dry socket," and to methods of making and using same. Of special import is a new vehicle used in the compositions.

Glycyrrhetinic acid and its active isomers; pharmaceutically acceptable salts thereof, such as the non-toxic alkali metal salts, e.g. the sodium salt of glycyrrhetinic acid; pharmaceutically acceptable esters thereof, e.g. glycyrrhetinic acid hydrogen succinate (see Patent 3,070,623) and glycyrrhetinic acid aminoethanol ester (see Patent 3,070,624); pharmaceutically acceptable glycyrrhetinic acid acryl derivatives e.g. acetyl glycyrrhetinate; xanthoglabrol (see Patent 3,066,072); pharmaceutically acceptable salts of xanthoglabrol with organic bases, e.g. the piperazine, protamine, purine and N-methylglucamine salts; and pharmaceutically acceptable salts of xanthoglabrol with inorganic bases, such as alkali metal salts, e.g. xanthoglabrol sodium salt; have a marked effect in suppressing inflammation. They also potentiate other therapeutics so as to achieve a synergistic effect when employed admixed therewith in a single composition.

It is an object of the present invention to provide a composition containing an active ingredient, e.g. glycyrrhetinic acid, xanthoglabrol or one of their pharmaceutically acceptable derivatives, such as those suggested heretofore, which composition will permit the slow release over an extended period of time of the active ingredient. A further object is to provide an inert and insoluble carrier for the active ingredient. The prime object, however, is to formulate compositions for the treatment of "dry socket." Still further objects will be apparent from the ensuing description.

One of the most distressing complications which may be encountered in dental extraction is "dry socket" which can cause excruciating pain. Although the aetiology of this condition is unknown, it would appear to be closely associated with the absence or loss of the blood clot, which in turn is linked with excessive vascular constriction probably caused by the large-scale use of drugs and possibly aggravated by sclerosis of the bone.

Many medicaments have been tried, the most popular to date being zinc oxide and eugenol, or zinc oxide and "Dentalone." Although these relieve pain, they have the disadvantage of leaving a large empty socket which requires repeated packing, and the cure is rather slow and not always effective. To avoid this there is provided according to the present invention, a composition in the form of a paste, which will not only relieve pain, but will encourage organisation of the socket and suppress inflammation, and which provides a vehicle which can be easily controlled and will slowly release the active therapeutic substances, while at the same time preventing infection in the surrounding area which is, of course, very prone to infection since it is surrounded by a large amount of bacterial flora.

The new composition, according to the present invention, comprises a pharmaceutical agent, preferably glycyrrhetinic acid and/or one of its active isomers and/or derivatives and/or xanthoglabrol and/or its derivatives together with a plastic material of the polythene family with a suitable plasticizer, e.g. lithium hydroxy stearate, in a miscible type of oily or fatty material, e.g. liquid petrolatum. In the following discussion of this invention, each reference to glycyrrhetinic acid is understood to include additionally or in the alternative one of its active isomers and/or one or more of its pharmaceutically acceptable derivatives, such as a salt, ester or acyl derivative thereof. Each reference to xanthoglabrol likewise is understood to include additionally or in the alternative one or more of its pharmaceutically acceptable derivatives such as a salt thereof.

For the preparation of compositions according to the present invention, the oily or fatty material, such as liquid paraffin, e.g. liquid petrolatum, and polythene (polyethylene) are melted together at a temperature of from about 130° to 200° C., but below the decomposition or boiling point of either and preferably at about 180° C. with continuous stirring. The polythene may be added to the pre-heated oily or fatty material either portionwise or continuously or in one amount. The formed liquid admixture is permitted to cool naturally, i.e. in an ambient atmosphere of room temperature (20° to 30° C.) and atmospheric pressure, to about 65° C., at which temperature platicizer, e.g. lithium hydroxy stearate, for the polythene is added gradually to said liquid admixture with constant stirring followed by the remaining ingredients, such as active ingredients, e.g. glycyrrhetinic acid or xanthoglabrol, while still stirring. It is critical that the plasticizer and the active ingredients be added at a temperature which is below their respective decomposition points. The plasticizer must be added at a temperature no higher than about 65° C. and the active ingredients must be added at a temperature no higher than about 65° C.

The polythene is that which is known as the branched chain (as opposed to "linear") or the low-density type, e.g. Bakelite DYNH or Alkathene 20. Preferred polythene has a density from 0.910 to 0.925, but medium density, i.e. from 0.926 to 0.940, polythene can also be employed. Although a crystallinity from 45 to 55% is desirable, the crystallinity can vary considerably as long as the polythene is not completely amorphous. It is also preferred that the polythene have a melting point between 100° and 120° and a molecular weight between 20,000 and 30,000. Alkathene 20 has a molecular weight of 24,000, a density of 0.92 gram/cubic centimeter, a refractive index of 1.52, a melting point between 110° and 120° C., and a decomposition temperature between 280° and 300° C.; it is soluble (at 60° to 75° C.) in many aromatic, aliphatic and halogenated hydrocarbons, but only slightly soluble in polar solvents. Bakelite DYNH has a molecular weight of about 21,000, a melting point of 110° C., a crystallinity of from 50 to 51 percent, a melt viscosity of 1,000,000 poises and a densiy of 0.92.

The polythene is preferably used in powdered or granular form but this is not essential and only serves to reduce the time necessary for dissolving the polythene in the oily or fatty material. It is to be understood that when the final viscosity of the vehicle is the greater, the greater is the molecular weight and/or crystallinity of the polythene used.

It is essential that the compositions be prepared with a plasticizer for the polythene. Any therapeutically acceptable inert (with respect to constituents) plasticizer for polythene may be employed.

A further essential ingredient for the preparation of the compositions of this invention is an oily or fatty mate-